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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,937	06/30/2000	MARIA EUGENIA MEIRINHOS DA CRUZ	249-119P	2705

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EXAMINER
KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/25/2003 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/529,937	Applicant(s) Da Cruz
	Examiner Gollamudi Kishore	Art Unit 1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 15, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-25 and 27-42* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-25 and 27-42* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request for the extension of time and amendment filed on 5-15-03 are acknowledged.

Claims included in the prosecution are 23-25 and 27-42.

Claim Rejections - 35 U.S.C. § 102

1. **The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:**

> **A person shall be entitled to a patent unless –**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

2. **Claims 23-24 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/31970 of record.**

WO discloses liposomal formulations containing trifluralin; the liposomes are made of phosphatidylcholine. Since the process of preparation in the prior art results in a liposome population of different sizes, the reference meets the requirements of dependent claims (note the abstract and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicants argue that WO is directed to a method of preparing a predetermined active agent stock solution for liposomal microencapsulation of active agent

for agricultural uses and not directed to pharmaceutical uses of liposomal compositions. These arguments are not found to be persuasive for the following reasons. First of all, instant claims are composition claims and the intended use has no significance in the composition claims. Secondly, both instant composition and the prior art composition teach the same active agent, trifluralin encapsulated in liposomes containing phospholipids. If trifluralin is dangerous to humans, as argued by applicants, then it should be dangerous whether it is in instant composition or prior art composition (which is the same). It is interesting to note that applicants themselves use the term, 'pesticide' (claim 25) just as in the reference. Applicants argue that the present invention as claimed in claims 23, 24 and 39 relates to liposomal formulations of different sizes and different physical properties, different lipid and drug ratios and different drug quantities. These arguments are not found to be persuasive since as pointed out before, said claims do not recite any specific drug amounts or specific lipids. With regard to the sizes and arguments based on liposomes obeying Gaussian distribution as also pointed out before, instant claims recite "mixture of distinct liposome populations of particles with distinct mean diameters respectively bigger and lower than 100 nm" and prior art liposomes are mixed population and therefore, meets the requirements of instant claims. Arguments based on Gaussian distribution thus, are not pertinent. Furthermore, since according to instant claims the liposomal sizes can be anywhere from above 400 to below 100 and as applicants themselves admit on page 6 of their response that "because of the large numbers of particles in any given population, a

Gaussian type distribution prevails", the prior art process results in liposomes having different diameters and therefore, reads on instant claims irrespective of the process by which they are prepared.

Claim Rejections - 35 U.S.C. § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

4. Claims 23-24 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's statements of prior art in view of Steck (4,186,183), Rao (4,594,241) individually or in combination or vice versa.

Applicant in the paragraph bridging pages 3 and 4 of the specification indicate that the herbicide, trifluralin is a well-known anti-leishmania drug.

Steck teaches liposomal carriers for the treatment of leishmaniasis (note the abstract). According to Steck the liposomes are taken up rapidly by cells and intra-cellular lysosomes of the reticuloendothelial system and that the characteristics of liposomes suggested that they might have a potential for application of carriers for anti-leishmania agents. Steck also teaches that the cells and tissues in which the liposomes are readily taken

up are the very locations in which the Leishmania organisms predominantly reside (note col. 2, lines 6-26). The anti-leishmania drug taught by Steck however, is not the claimed drug.

Rao similarly teaches the effectiveness of the liposomally encapsulated anti-leishmania drugs against this organism (note the abstract, examples and claims). The anti-leishmania drug taught by Rao however, is not the claimed compound.

The use of the liposomes as carriers of trifluralin would have been obvious to one of ordinary skill in the art because of effectiveness of liposomes as carriers of anti-leishmania drugs taught by Steck and Rao. Alternately, the use of trifluralin in the liposomes of Steck or Rao would have been obvious to one of ordinary skill in the art with the expectation of obtaining the benefits of the liposomes since trifluralin is a art known anti-leishmania drug.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicants argue that Steck, Rao do not teach trifluralin. The examiner agrees, but points out that both Steck, and Rao are directed to the treatment of leishmania using liposomal compositions and the effectiveness of liposomes as carriers for anti-leishmania drugs. Therefore, one of ordinary skill in the art would be motivated to use art known anti-leishmania drug, trifluranin with a reasonable expectation of success. Applicants' arguments with regard to sizes have been addressed above.

8. Claims 23-25 and 27-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's statements of prior art in view of Steck (4,186,183), Rao (4,594,241)

individually or in combination or vice versa as set forth above, further in view of GB 2 002 319: or WO 95/31970 cited above, further in view of GB 2 002 319.

Neither Steck nor Rao nor WO teach the dehydration of the liposomes and hydrating again.

GB teaches that liposomes can be dehydrated for storage as a stable powder. According to GB such dehydrated powders can be stored for long periods and from which a dispersion of liposomes can be reconstituted (note the abstract).

Dehydrating the liposomes of Steck or Rao or WO would have been obvious to one of ordinary skill in the art because GB teaches that the liposomal powders can be stored for a long time.

Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants argues that the use of an anti-sublimating agent in the process described and claimed in claim 25 and those claims dependent thereon is nowhere taught or even suggested in any of the prior art. The rationale behind this argument is unclear to the examiner since GB clearly teaches that sugars protect the liposomes during dehydration and rehydration procedure. The references of Unger (6,416,740) and Horikoshi (4,348,384) which teach that lyophilization is a sublimation process are cited of interest in this context (note col. 3, line 44 et seq., of Unger and col. 6, lines 38-42 of Horikoshi).

5. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

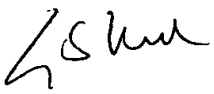
The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.



Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

July 21, 2003